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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,407	01/24/2002	Lydie Meheus	INNS:011-1 11362.0011.DVU	3304
23369	7590	11/15/2006	EXAMINER ZEMAN, ROBERT A	
HOWREY LLP C/O IP DOCKETING DEPARTMENT 2941 FAIRVIEW PARK DRIVE, SUITE 200 FALLS CHURCH, VA 22042-7195			ART UNIT 1645	PAPER NUMBER

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/056,407	<b>Applicant(s)</b> MEHEUS ET AL.	
	<b>Examiner</b> Robert A. Zeman	<b>Art Unit</b> 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,24-26 and 35-42 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,24-26 and 35-42 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                           | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

### **DETAILED ACTION**

The amendment and response filed on 5-15-2006 are acknowledged. Claim 1 has been amended. Claims 7-9, 11-13, 23 and 27-34 have been canceled. Claims 37-42 have been added. Claims 1, 24-26 and 35-42 are pending and currently under examination.

#### ***Objections Maintained***

##### ***Specification***

The trademark Prospin<sup>TM</sup> is properly capitalized but is not accompanied by the requisite generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

#### ***Claim Rejections Withdrawn***

The new matter rejection of claims 1, 23-26 and 35-36 under 35 U.S.C. 112, first paragraph, based on the amendment to claim 1 to recite “asymmetrical dimethyl arginine” is withdrawn in light of the amendment thereto.

The new matter rejection of claims 1, 23-26 and 35-36 under 35 U.S.C. 112, first paragraph, based on the amendment to claim 1 to recite “symmetrical dimethyl arginine” is withdrawn in light of the amendment thereto.

The rejection of claim 23 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn. Cancellation of said claim has rendered the rejection moot.

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The rejection of claims 1, 24, 26 and 35-36 under 35 U.S.C. 102(b) as being anticipated by Rajpurohit et al. (Biochim Biophys Acta. 1992 July 31; 1122(2) pages 183-188) is withdrawn in light of the amendment thereto.

***Claim Rejections Maintained***

***35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 24-26 and 35-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in the previous Office action in the rejection of claims 1, 24-26 and 35-36. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

**Applicant argues:**

1. The amended claims now require that the claimed peptide be able to react with antibodies and wherein the methylation is crucial to said reaction. Hence the claims now recite a function.
2. The specification discloses several peptides that comprise species of the claimed genus.
3. The specification discloses the claimed XG motif is required for recognition by

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antibodies in sera from patients with SLE.

4. Antibodies responsible for the deleterious effect in SLE require methylation of an XG motif present within the claimed antigenic peptides.

Applicant arguments have been fully considered and deemed non-persuasive.

With regard to Points 1 and 2, the instant claims encompass peptides that bind to any antibody from an SLE patient. The specification does not provide support for this vast genus as it provides limited guidance with regard to what other amino acids must be present in addition to the methylated XG motif. Moreover, the specification is remiss in describing which antibody:antigens are predicated on the methylated XG motif. Finally, the limited number of examples disclosed in the specification does not qualify as a representative number of species as required the written description requirement.

With regard to Points 3 and 4, it is noted that the features upon which applicant relies (i.e., the antibodies which bind the claimed peptides cause the deleterious effects of SLE) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The claims are drawn to a vast genus of branched peptides containing less than 50 amino acids comprising at least one XG dimer wherein X stands for N<sup>G</sup>- mono- or N<sup>G</sup>-N<sup>G</sup>-dimethylated arginine, or N<sup>G</sup>'-N<sup>G</sup>'-dimethylated arginine, that are specifically recognized by antibodies present in sera from patients with SLE wherein said methylation is crucial to antibody:peptide reaction.

To fulfill the written description requirements set forth under 35 USC § 112, first

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paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of peptides specifically recognized by certain antibodies, Applicant must adequately describe the peptides to which the antibodies bind. That description must include a description of the immunoepitopes specifically recognized by each of the recited “antibodies”. The specification, however, does not disclose distinguishing and identifying features of a representative number of members of the genus of peptides to which the claims are drawn, such as a correlation between the structure of the peptide and its recited function, so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of antibodies. Moreover, the specification fails to disclose which amino acid residues are essential to the function of the peptide, or which amino acids might be added, replaced or deleted so that the resultant peptide retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant peptide retains the activity of its parent. Therefore, the specification fails to adequately describe at least a substantial number of members of the genus of peptides to which the claims refer; and accordingly the specification fails to adequately describe at least a substantial number of members of the claimed genus of antibodies.

MPEP § 2163.02 states, “[a]n objective standard for determining compliance with

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the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

*The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement* (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure

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of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was “ready for patenting” by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, “[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus” (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by the teachings of Skolnick et al., the art is unpredictable. Skolnick et al. (*Trends in Biotechnology* **18**: 34-39, 2000) discloses the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, *Sequence-based approaches to function prediction*). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see, in particular, the abstract and Box 2). Thus, one skilled in the art would not accept the assertion, which is based only upon an observed similarity in amino acid sequence, that a variant of the polypeptide a given peptide would necessarily bind to a given antibody. Therefore, because the art is unpredictable, in accordance with the



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*Guidelines*, the description of claimed antibodies is not deemed representative of the genus of peptides to which the claims refer.

Finally it should be noted that the courts have recently decided in *Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin* (CAFC, 02-1187, 1/20/2004) that:

a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen.

Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen.

Moreover, as the scope of the claims includes numerous structural variants, and the genus is highly variant, recitation of the limitation "containing less than 50 amino acids comprising at least one XG dimer wherein X stands for N<sup>G</sup>- mono- or N<sup>G</sup>-N<sup>G</sup>-

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dimethylated arginine or N<sup>G'</sup>-N<sup>G'</sup>-dimethylated arginine and said peptide is able to react with antibodies and with said methylation being crucial for the reaction..." alone is insufficient to describe the genus. Thus, Applicant has not described a function that is shared by the claimed branched peptide that would adequately describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

***35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 24, 26 and 35-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Rawal et al. (Biochemica et Biophysica Acta Vol. 1248, 1995 pages 11-18) for the reasons set forth in the previous Office action.

**Applicant argues:**

1. Rawal only discloses a cyclized peptide with the sequence CGKCRKC.
2. Rawal describes the enzymatic methylation of polypeptides and conclude the function of Protein A1 methylation "may modulate the nucleic binding properties".
3. Rawa; does not disclose antibody binding affinities or link RG methylation to autoimmune or other diseases (specifically SLE).

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Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, Rawal disclose multiple peptides which meet the limitations of the instant claims (see abstract and Tables 1 and 2 on page 13).

With regard to Points 2 and 3, since the peptides disclosed by Rawal et al. have the same "sequence" as those recited by in the instant claims, it is deemed, in absence of evidence to the contrary, both would necessarily have the same immunological properties.

As outlined previously, Rawal et al. disclose branched peptides of less than 50 amino acids comprising at least one XG dimer (see abstract and page 13 for example). Consequently, Rawal et al. anticipate all the limitations of the instant invention.

### ***New Grounds of Rejection***

#### ***35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 24-26 and 35-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the use of the term "react" with regard to antibodies and the claimed peptides. It is unclear, as said term is not specifically defined in the specification, what process other than "binding" is meant to be encompassed by the term "react".

***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

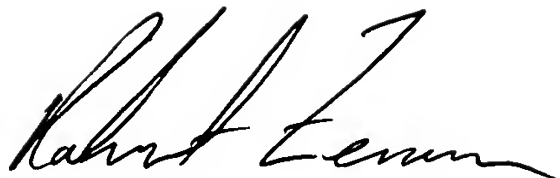
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272 0866. The examiner can normally be reached on Monday – Thursday, 8am – 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272 0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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ROBERT A. ZEMAN  
PRIMARY EXAMINER

November 11, 2006